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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/109,082	07/02/1998	JUDITH MELKI	2121-140P	3158

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BIRCH STEWART KOLASCH & BIRCH
PO BOX 747
FALLS CHURCH, VA 22040-0747

EXAMINER
HAYES, ROBERT CLINTON

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 07/29/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/109,082	Melki et al
Examiner	**Art Unit**
Robert C. Hayes, Ph.D.	1647

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *May 10, 2002* .

2a) ☐ This action is **FINAL.** 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *21, 23, 30-34, 36, and 40-65* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *21, 23, 30-34, 36, and 40-65* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 5/10/02 has been entered.

2. The rejection of claims 40-52 under 35 U.S.C. 112, second paragraph, as being indefinite as it relates to SEQ ID NO:13 is withdrawn due to the amendment of the claims.

3. The rejection of claim 21 under 35 U.S.C. 112, second paragraph, as being indefinite and incomplete for the recitation of "an amplification reaction", is withdrawn due to an amendment of the claim.

4. The rejection of claim 31 under 35 U.S.C. 112, second paragraph, as being indefinite and lacking proper antecedent basis for the recitation of "said motor neuron disorder", is withdrawn due to Applicants' arguments.

5. The rejection of claims 23 & 40-63 under 35 U.S.C. 112, second paragraph, as being indefinite for SEQ ID NO:21 being an amino acid sequence vs. a gene sequence, is withdrawn due to the amendment of the claims.

6. Applicant's arguments filed 5/10/02 have already been fully considered in the Advisory Action of 3/11/02 (Paper NO: 22), but were not deemed to be persuasive.

7. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

8. Claims 23, 30-32, 36, 53 & 65 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention, for the reasons made of record in Paper No: 20, and as follows.

No proper antecedent basis nor conception in context with that described within the specification at the time of filing the instant application remains apparent for the recitation, "a Survival Motor Neuron disorder"(i.e., as it relates to claims 30-32 & 65). Note that "*Survival* Motor Neuron *disorder*" is not equivalent to "Survival Motor Neuron *gene*", nor equivalent in

scope to the specific disease states listed within the specification or recited, for example, in claims 36 or 40, or for any generic motor neuron disorder; thereby, still constituting new matter.

No proper antecedent basis nor conception in context with that described within the specification at the time of filing the instant application exists for the recitation, "comprises at least 9 nucleotides within... SEQ ID NO:22", versus SEQ ID NOs: 12 or 13 of Figure 3 (i.e., as it relates to claims 23 & 53). For example, see page 19 of the specification. In addition, the hybridization products of claim 53 (i.e., original claim 22) are not contemplated for SEQ ID NO:22, as was previously made of record for SEQ ID NO:21, which alternatively "represents... the entire SMN gene" (see pg. 20 of the specification); thereby, still constituting new matter because of the different scope still encompassed by the current claim language.

No proper antecedent basis nor conception in context with that described within the specification at the time of filing the instant application exists for the broader concept and scope of using SSCP analysis for any random pairs of primers contained in SEQ ID NOs: 12 or 22" (i.e., as it relates to claims 30, 36 & 65), versus the primers depicted as SEQ ID NOs: 5-6 and 7-8, as contemplated in Example 10. Note that this is the only place in the specification describing SSCP analysis; thereby, constituting new matter.

9. Claims 21, 23, 30-34, 36, 40-65 stand rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of detecting specific motor disease states related to specific mutations of specific nucleotide sequences (i.e., by SEQ ID NO) using

structurally definable probes or pairs of probes (i.e., by SEQ ID NO) and known restriction enzymes to generate detectable and definable polymorphisms, does not reasonably provide enablement for any generic method, or kit, that does not identify the specific disease state being detected, using structurally uncharacterized probes that may or may not identify specific portions of undefined or unknown genes, or unknown and undescribed polymorphisms thereof. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims, for the reasons made of record in Paper NOs: 18 & 20, and as follows.

Applicants argue that they have amended the claims to recite "at least one of said primers is contained within the sequence...", and in which "both primers are in the sequence of nucleotides 921 to 1469 of SEQ ID NO:12", etc. However, in contrast to Applicants' assertions that the invention is now enabled, without identifying what pair of primers to be used to detect known and defined gene "truncations, deletions or mutations" in "kits" or in the recited "methods", one of ordinary skill in the art would not know how to make and use Applicants' invention, as currently claimed, because undefined disorders/defects must possess some defined structure/polymorphisms, etc. by which the skilled artisan could then detect any putative difference using known primer pairs that bind to opposite strands of a known sequence, in order for any PCR amplification to then putatively occur. For example, any random primer within a given sequence coding in the same direction would give rise to only a single strand, and therefore, make it impossible to amplifying a given polymorphism, etc. because both strands

must be present to accomplish such, if known and defined. In other words, the current claims merely constitute an invitation for others to discover what pairs of primers may work to generate unknown and undescribe polymorphisms, etc. that may characterize unknown and undefined disorders putatively manifested by a defective SMN gene. Note that the instant rejection is consistent with that held by the courts in *Novo Nordisk v. Genentech*, 42 USPQ2d 1001 (Fed. Cir. (N.Y.), 1997) in that:

"[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable".

Clearly, that claimed is not adequately described in the instant specification, nor do the current claims specifically recite what exactly is required in a "kit" or in a claimed "method" for detecting otherwise unknown and undefined disorders using random and unknown pairs of primers; thereby, requiring undue experimentation to discover how to make and use Applicants' invention, by definition, as previously made of record; which is consistent with that held by courts in *In re Wands, 8 USPQ2d 1400 (CAFC 1988)* regarding the Foreman factors, *Ex parte Maizel*, and the teachings of Rudinger previously made of record. Therefore, Applicants' arguments remain not persuasive for the reason made of record.

10. Claims 30-31, 36, 48 & 65 stand rejected under 35 U.S.C. 112, second paragraph, as being indefinite and incomplete for failing to particularly point out and distinctly claim the

subject matter which applicant regards as the invention, for the reasons made of record in Paper NOs. 18 & 20, and as follows.

It remains unknown what metes and bounds define " a Single-Stranded Conformation Polymorphism (SSCP)", since no such SSCP conditions, conformations nor polymorphisms are recited in the claims; thereby, still being incomplete especially for use of any random "said primers", etc. Note that Example 10 only describes how to use the primers depicted as SEQ ID NOs: 5-6 and 7-8 in a specific method, which in itself does not define what constitutes a "SSCP analysis", wherein the term "analysis" is further ambiguous and defines no known parameters.

11. Claims 30-33, 36 & 65 stand rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps, for the reasons made of record in Paper NOs. 18 & 20. See MPEP § 2172.01.

The omitted steps remain what distinguishes "is indicative of a Survival Motor Neuron disorder" (i.e., as it relates to claims 30 & 65) from "is indicative of a Spinal Muscular Atrophy" (i.e., as it relates to claim 31) when identical steps are recited and the differences that distinguishes a "Survival Motor Neuron disorder" from a "Spinal Muscular Atrophy" are not defined or known; thereby, being indefinite and confusing. For example, does a specific mutation define each of these putatively distinct disorders, and if yes, what and where is such specifically described, or recited in the claims? Likewise, claim 33 still recites "detecting the presence or absence of Spinal Muscular Atrophy", while claim 36 still recites "detecting the

presence or absence of Arthrogryposis Multiplex Congenita", which remain not described or known; thereby, still constituting an incomplete method for detecting such.

12. Claims 23, 33-34 & 53 stand rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, for the reasons made of record in Paper NOs. 18 & 20 and as follows.

Applicants argue that "Sambrook et al. indeed is *but one example*, but the skilled artisan could determine stringent conditions"[emphasis added]. However, this is not an enablement rejection but a rejection for indefiniteness, in which Applicants essentially admit that the term, "stringent conditions" is open ended, and therefore, not defined. Therefore, Applicants' arguments remain not persuasive because it still remains unknown what metes and bounds "stringent hybridization conditions" entail, in that it is unknown whether low, moderate or high stringent conditions are envisioned; nor what exactly defines these conditions, as previously made of record.

13. Claims 43, 47-48 & 64 stand rejected under 35 U.S.C. 112, second paragraph, as being indefinite and incomplete for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, for the reasons made of record in Paper NOs. 18 & 20.

It remains unknown what metes and bounds "analyzing" entails, since no restriction enzyme to determine such is recited in claim 47, and in which no "amplification reaction" remains defined for claim 64, etc., and for the reasons previously made of record.

14. Claims 53 & 23 are rejected under 35 U.S.C. 102(b) as being anticipated by Stratagene Cloning Systems Catalog (1994).

Stratagene disclose a kit (catalog #300385) that comprises purified random 9-mer oligonucleotide primers/probes (i.e., "at least 9 nucleotides within a sequence of SEQ ID NO:22"), which also inherently hybridize to SEQ ID NOs: 1,2, 10-13 or 22. In that Stratagene's kit comprises the same products as that recited in claim 53, and because any intended uses of detecting SMA carries no patentable weight, as claimed, the limitations of claim 23 are also met.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Robert Hayes whose telephone number is (703) 305-3132. The examiner can normally be reached on Monday through Thursday, and alternate Fridays, from 8:30 AM to 5:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz, can be reached on (703) 308-4623. The fax phone number for this Group is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Robert C. Hayes, Ph.D.
July 18, 2002

Gary L. Kunz